SARS-CoV-2: Comparing the immune response in children and adults

Written by Lori Uildriks on November 16, 2020 — Fact checked by Rita Ponce, Ph.D.

A recent study from researchers at Columbia University Irving Medical Center in New York demonstrated distinct differences between the antibody responses of children and adults with COVID-19. In particular, the differences were seen in the type, amount, and neutralizing activity of antibodies.

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severity is milder in children than it is in adults.

The majority of children with a SARS-CoV-2 infection are asymptomatic or display mild symptoms. Most often, these are cough, fever, or gastrointestinal symptoms.

Infants less than 1 year of age and children with certain underlying medical conditions are at greater risk of developing a severe form of COVID-19.

In some rare cases, children who develop COVID-19 exhibit a medical condition called multisystem inflammatory syndrome in children (MIS-C). This condition causes inflammation of the eyes, skin, brain, kidneys, lungs, heart, or gastrointestinal tract, sometimes beginning weeks after a person has contracted SARS-CoV-2.

Adults are more likely than children to manifest with severe or critical illness from COVID-19, especially those who are older or those with certain underlying medical conditions, such as obesity, type 2 diabetes, chronic kidney disease, and cancer.

Severe illness often requires hospitalization and may include management of complications such as acute respiratory distress syndrome (ARDS), pneumonia, blood clots, acute kidney injury, sepsis, or cardiomyopathy.

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Scientists do not yet understand why children and adults respond so differently to a SARS-CoV-2 infection.

The recent study set out to investigate the differences in immune responses to SARS-CoV-2 between adults and children. The scientists examined a range of immune components.

People with a SARS-CoV-2 infection and people who have recovered from mild disease display antibodies specific to proteins on the novel coronavirus: spike (S) proteins and nucleocapsid (N) proteins. The S protein of the virus binds to the cell's receptor, allowing viral entry. The N protein is necessary for replication of SARS-CoV-2.

Anti-S antibodies can effectively neutralize viral activity. Studies investigating their use in vaccines and for treatment of severe COVID-19 disease are currently underway.

In the new study, which appears in *Nature Immunology*, researchers investigated the type and neutralizing activity of antibody response in a total of 32 adults and 47 children with COVID-19 seen at the New York-Presbyterian/Columbia University Irving Medical Center hospital and the Morgan Stanley Children's Hospital of New York from March to June 2020.

The study involved two groups of adults and two groups of children. One group of adults comprised 19 convalescent plasma donors (CPD) who recovered from mild COVID-19 respiratory illness without requiring hospitalization. The second adult group included 13 people who were hospitalized with severe COVID-19 ARDS (COVID-ARDS).

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In both the COVID-ARDS and MIS-C groups, participants had high levels of inflammatory markers called interleukin 6 and C-reactive protein. Those in the COVID-ARDS group also experienced significantly increased levels of ferritin and lactate dehydrogenase than those in the MIS-C group.

Only two children developed ARDS: one in the non-MIS-C and one in the MIS-C group. This illustrates the difference in inflammatory responses and clinical symptoms between adults and children in response to COVID-19, according to the authors of the study.

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Different antibody responses

Both adult groups generated anti-S antibodies: immunoglobulin G (IgG), immunoglobulin M (IgM), and immunoglobulin A (IgA) antibodies. There were significantly greater concentrations of these antibodies in the COVID-ARDS group.

In contrast, in the two groups of children and in CPD adults, there was a similar pattern of anti-S antibodies: a predominance of IgG and low

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Results showed significantly lower neutralizing activity in the two pediatric groups compared with the two adult groups. There were no differences in neutralizing activity between the two pediatric groups, but the adult COVID-ARDS group demonstrated the highest neutralizing potency across all four groups.

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COVID-19 antibody response in children was predominantly anti-S IgG antibodies and possessed the lowest amount of neutralizing activity.

Pediatric patients affected with different severities of COVID-19 showed similar antibody patterns, neutralizing activity, and concentrations. In adult groups, the patients with the most severe disease (ARDS) had the greatest concentration and variety of anti-SARS-CoV-2 antibodies with the highest neutralizing activity.

“This is a new infection for everybody, but children are uniquely adapted to see pathogens for the first time. That’s what their immune system is designed to do. Children have a lot of naive T cells that are able to recognize all sorts of new pathogens, whereas older people depend more on our immunological memories. We’re not as able to respond to a new pathogen like children can,” explains study co-lead Donna Farber, Ph.D.

Because the immune system of children successfully clears the virus, this might result in reduced functional antibody response compared with adults. Differences in viral clearance could also explain why children usually experience less severe disease from COVID-19.

A milder disease course in children is also consistent with lower concentrations of anti-N antibodies. This is because N proteins are only released following the destruction of cells that are infected by SARS-CoV-2.

According to Farber, “There is a connection between the magnitude of your immune response and the magnitude of the infection: The more severe the infection, the more robust the immune response, because you need to have more immune cells and immune reactions to clear a higher dose of a pathogen.”

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Farber adds, “If the innate response is really strong, that can reduce the viral load in the lungs, and the antibodies and T cells of the adaptive response have less to clear up.”

Also, children may produce less angiotensin-converting enzyme 2 (ACE2) receptors in the cells lining their airways than adults. ACE2 is a protein on human cell surfaces through which SARS-CoV-2 gains entry into the cells.

“There are still all these issues that we have very little information about,” says co-lead author Matteo Porotto, Ph.D. “The interaction between the virus and the host is the reason why we see so much diversity in responses to this virus, but we don’t understand enough about this virus yet to really determine what leads to severe disease and what leads to mild disease.”

More studies are needed to identify differences in adult and pediatric immune responses to COVID-19 to understand how disease or protection occurs in response to exposure to SARS-CoV-2. These results could profoundly impact the development of age-related testing and protection to control this unrelenting pandemic.

For live updates on the latest developments regarding the novel coronavirus and COVID-19, click here.

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